

We claim:

1. Agonist molecules which specifically bind to or interact with human G-CSF receptor to stimulate cell proliferation and differentiation.
- 5 2. The agonist molecules of claim 1 which stimulate proliferation and differentiation of neutrophils or its progenitor cells.
3. Agonist molecules which specifically bind to or interact with human G-CSF receptor and dimerize the receptor or activate phosphorylation of kinases associated with the receptor to stimulate cell proliferation and differentiation.
- 10 4. The human G-CSF receptor of claim 1 which is a native human G-CSF receptor, or its mutants with substitutions, insertions or deletions.
5. The agonist molecules of claims 1 or 3 which interact with the extracellular portion of human G-CSF receptor.
- 15 6. The agonist molecules of claim 5 which interact at a region between amino acid residues 1-603 (SEQ ID NO: 27) of the G-CSF receptor.
7. The extracellular portion of human G-CSF receptor of claim 5 which is the extracellular portion of human G-CSF receptor of claim 4.
8. The agonist molecules of claims 1 or 3 which are monoclonal antibodies, or fragments, homologues or analogues thereof, or peptides or organic compounds.
- 20 9. The fragments of claim 6 which are F(ab)'₂, Fab or scFv.
10. The monoclonal agonist antibodies of claim 8 which include mAb163-93 and mAb174-74-11.
- 25 11. Agonist molecules which bind to the same epitope as either the monoclonal antibody mAb163-93 or mAb 174-24-11.

12. Agonist molecules of claims 1 or 3 which are capable of stimulating the proliferation of human or mouse cells expressing the human G-CSF receptor as determined in an *in vitro* proliferation assay.

5 13. The monoclonal agonist antibody mAb163-93 of claim 10, which belongs to IgG1 subclass, wherein the CDRs of the variable region heavy chain include one or more of the following amino acid sequences:

CDR1: Asn Tyr Gly Met Asn (SEQ ID NO: 15)

CDR2: Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Gly Asp Phe Lys Gly (SEQ ID NO: 16)

10 CDR3: Glu Gly Phe Tyr Gly Gly His Pro Gly Phe Asp Tyr
(SEQ ID NO: 17)

Or the CDRs of the variable region light chain include one or more of the following amino acid sequences:

15 CDR1: Lys Ser Ser Gln Ser Leu Leu Ser Ser Arg Thr Arg Lys Asn Tyr
Leu Ala (SEQ ID NO: 18)

CDR2: Trp Ala Ser Thr Arg Glu Ser (SEQ ID NO: 19)

CDR3: Lys Gln Ser Tyr Asn Leu Arg Thr (SEQ ID NO: 20)

14. The monoclonal agonist antibody mAb174-74-11 of claim 10, which belongs to IgG2a subclass, wherein the CDRs of the variable region heavy chain include one or more of the following amino acid sequences:

CDR1: Ser Tyr Ala Met Ser (SEQ ID NO: 21)

CDR2: Gly Ile Ser Ser Gly Gly Ser Tyr Ser Tyr Tyr Pro Gly Thr Leu Lys Gly (SEQ ID NO: 22)

CDR3: Glu Ala Tyr Asn Asn Tyr Asp Ala Leu Asp Tyr (SEQ ID NO: 23)

25 or CDRs of the light chain variable region include one or more of the following amino sequences:

CDR1: Arg Ala Ser Ser Ser Val Thr Tyr Val His (SEQ ID NO: 24)

CDR2: Ala Thr Ser Asn Leu Ala Ser (SEQ ID NO: 25)

CDR3: Gln Gln Trp Thr Ser Asn Pro Phe Thr (SEQ ID NO: 26)

15. Hybridoma cell lines producing the monoclonal agonist antibodies,
5 fragments, homologues, analogues or peptides of claim 8.
16. The hybridoma cell lines of claim 13 which are hybridoma cell lines 163-
93 or 174-74-11.
17. DNA sequences encoding monoclonal agonist antibodies, fragments,
homologues, analogues or peptides of claim 8.
- 10 18. Gene delivery systems including DNA sequences encoding monoclonal
agonist antibodies, fragments, homologues, analogues or peptides of claim
8.
19. Gene delivery systems including one or more of the DNA sequences
shown in SEQ ID NOS: 15 through 26.
- 15 20. Gene delivery systems of claim 16 wherein said systems include viral
vectors, plasmids, or non-vector delivery systems.
21. A method of treating neutropenia comprising administering the molecules
of any of claims 1-3.
22. A method of treating neutropenia comprising administering the molecules
20 of claim 5.
23. A method of treating neutropenia comprising administering the molecules
of claim 8.
24. A method of screening a molecule for G-CSF agonist activity comprising
determining if the molecule can stimulate the proliferation of G-CSF-
25 dependent cells.

25. The method of claim 22 wherein the measurement is made using an *in vitro* assay.
26. The method of claim 23 wherein the assay method is an MTT-based colorimetric assay or an ^3H -thymidine uptake assay using cells expressing G-CSF receptor.
5
27. The G-CSF dependent cells of claim 22 which express proteins, or fragments thereof, having the sequence of the extracellular domain or its part of the G-CSF receptor on its cell membrane surface.
28. A method for detecting the human G-CSF receptor immunologically by means of antibodies of claim 8.
10
29. A method for immunological detection of a cell expressing the human G-CSF receptor on the cell surface by means of the antibodies of claim 8.
30. A method for detecting and determining a soluble human F-CSF receptor immunologically by means of antibodies of claim 8.